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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/442,489	11/18/99	VOGELSTEIN B	01107.78817

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EXAMINER	
VANDER VEGT, F	

ART UNIT	PAPER NUMBER
1644	10

DATE MAILED: 03/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/442,489	Applicant(s) Vogelstein et al
	Examiner F. Pierre VanderVegt	Group Art Unit 1644

☒ Responsive to communication(s) filed on *Dec 12, 2000*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), ~~or thirty days, whichever is longer,~~ from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-8* ~~is~~/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☒ Claim(s) *1* _____ is/~~are~~ allowed.

☒ Claim(s) *2-8* _____ ~~is~~/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- *SEE OFFICE ACTION ON THE FOLLOWING PAGES* ---

DETAILED ACTION

This application is a reissue of application serial number 08/452,654, which is a division of 08/289,548, which is a division of 07/741,940.

Claims 1-8 are currently pending in this application.

1. In view of the amendment filed December 12, 2000, only the following rejections are maintained.

Claim Rejections - 35 USC § 112

2. Claims 2-8 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It was stated previously: "The claims are drawn to a preparation of antibodies which bind to a human adenomatous polyposis coli (APC) protein which is the product of a mutant allele. The written description in this case only sets forth amino acid and nucleic acid sequences for human APC and the mutants identified in Table II, and therefore the written description is not commensurate in scope with the claims drawn to "mutants" comprising the full genus of any changes to the nucleic acid molecule defined by SEQ ID NO:1, whether it be silent or expressed as an alteration to the amino acid sequence of the encoded protein.

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111), clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See *Vas-Cath* at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see *Vas-Cath* at page 1115).

With the exception of the sequences encoding human APC and the mutants identified in Table II, the skilled artisan cannot envision the detailed structure of the encompassed nucleic acid sequences and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, ((CAFC,

1993) 25 USPQ 2d 1601) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*,((CAFC, 1991) 18 USPQ2d 1016).

Furthermore, In *The Reagents of the University of California v. Eli Lilly* ((CAFC, 1997) 43 USPQ2d 1398), the court held that a generic statement which defines a genus of nucleic acids without distinguishing that genus from others, except by their function, does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention."

The sole support for additional species of human APC is provided in the specification at column 5, lines 21-49 for example, where it is disclosed that mutations encompass any changes in the nucleotide sequence of APC alleles, the germline changes disclosed in Table IIA and in the disclosure of the point mutations in the APC gene so far discovered in sporadic colorectal cancers which are summarized in Table IIB. This is insufficient to support the recitation in the claims of "mutants" as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore, nucleic acid molecules which encode human APC and the mutants identified in Table II, but not the full breadth of the claims generically drawn to mutants of human APC, meet the written description provision of 35 USC 112, first paragraph.

Analysis of the number of mutant and wild-type PCR clones obtained from each of these tumors showed that in two of the four cases, the wild-type sequence was present in approximately equal proportions to the mutant. This was confirmed by RFLP analysis using flanking markers from chromosome 5q which demonstrated that only two of the ten tumors (T135 and T201) exhibited an allelic deletion on chromosome 5q. These results are consistent with previous observations showing that 20-40% of sporadic colorectal tumors had allelic deletions of chromosome 5q. Moreover, these data suggest that mutations of 5q21 genes are not limited to those colorectal tumors which contain allelic deletions of this chromosome."

Claim 3 is included because, although the claim recites a number of specific mutation loci, the claim is not limited to these loci. The claim is written in an open language format, reciting "wherein the mutant allele contains" (emphasis added for clarity) and therefore encompasses any change to the sequence, not just those at the recited loci."

Applicant's arguments filed December 12, 2000 have been fully considered but they are not persuasive.

Applicant contends that there is adequate written description in the instant specification for the full scope of the claimed invention because Applicant recites a number of APC mutants.

In order to bolster this position, Applicant recites these examples of APC mutants in the response. Applicants arguments are not persuasive for the following reasons. Briefly reiterating, the claims are drawn to a preparation of antibodies which bind to a human adenomatous polyposis coli (APC) protein which is the product of a mutant allele. Of the 13 mutants cited in Applicant's response of 12/12/2000, six are truncation mutants, IE polypeptides with a stop codon found earlier in the sequence than in the wild-type APC. Since the polypeptide sequence to that point is identical to wild-type, it is not clear how Applicant can make an antibody which can recognize the truncated form but not the wild-type. Further, Applicant alludes to a mutant disclosed at column 16, lines 52-56 which has an 800 bp nucleotide insert. There is no indication, however, that this translates into a mutation detectable at the amino acid level as the detection of this mutant was only at the DNA level. There is no information regarding the sequence of the insert and this insert may constitute only an intron-like sequence which is spliced out prior to protein expression. Accordingly, there is not sufficient disclosure of a representative number of species to satisfy the written description requirement.

Allowable Subject Matter

3. Claim 1 is allowed.

Conclusion

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

5. Papers related to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for official documents to be entered into the record for Art Unit 1644 is (703)305-3014.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to F. Pierre VanderVegt, whose telephone number is (703)305-6997. The Examiner can normally be reached Tuesday through Friday and odd-numbered Mondays (on year 2001 365-day calender) from 6:30 am to 4:00 pm ET. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ms. Christina Chan can be reached at (703)308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist, whose telephone number is (703)308-0196.

F. Pierre VanderVegt, Ph.D.
Patent Examiner
Technology Center 1600
March 12, 2001

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